Basic fibroblast growth factor inhibits osteogenic differentiation of stem cells from human exfoliated deciduous teeth through ERK signaling.

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Authors: B Li, C Qu, C Chen, Y Liu, K Akiyama, R Yang, F Chen, Y Zhao, S Shi

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Public Summary:
Stem cell-based craniofacial tissue engineering is a promising approach for craniofacial structure reconstruction. Stem cells from human exfoliated deciduous teeth are capable of differentiating into osteogenic/odontogenic cells, adipocytes, and neural cells. When transplanted subcutaneously into immunocompromised mice, SHED induced robust bone formation in vivo. Additionally, SHED effectively repaired critical-size orofacial defects both in mouse and minipig models, indicating that SHED are feasible cell source for orofacial regeneration. However, the mechanism of SHED-based tissue regeneration is not fully understood. Here, we showed that basic fibroblast growth factor (bFGF) treatment inhibited SHED-mediated mineralized tissue regeneration through activation of the extracellular signal-regulated kinase (ERK) 1/2 pathway. Activation of ERK1/2 signaling by bFGF treatment inhibited WNT/↑-catenin pathway, leading to osteogenic deficiency of SHED. ERK1/2 inhibitor treatment rescued bFGF-induced osteogenic differentiation deficiency. These data suggest that bFGF inhibits osteogenic differentiation of SHED via ERK1/2 pathway. Blockade ERK1/2 signaling by small molecular inhibitor-treatment improves bone formation of SHED after bFGF treatment.

Scientific Abstract:
Oral Diseases (2011) doi: 10.1111/j.1601-0825.2011.01878.x Objective: Stem cells from human exfoliated deciduous teeth (SHED) are a unique postnatal stem cell population capable of regenerating mineralized tissue and treating immune disorders. However, the mechanism that controls SHED differentiation is not fully understood. Here, we showed that basic fibroblast growth factor (bFGF) treatment attenuated SHED-mediated mineralized tissue regeneration through activation of the extracellular signal-regulated kinase (ERK) 1/2 pathway. Material and Method: The level of mineralized nodule formation was assessed by alizarin red staining. Expression levels of osteogenic genes, osteocalcin and runt-related transcription factor 2, were examined by RT-PCR. Subcutaneous implantation approach was used to assess in vivo bone formation. Downstream signaling pathways of bFGF were examined by Western blotting. Result: Activation of ERK1/2 signaling by bFGF treatment inhibited WNT/beta-catenin pathway, leading to osteogenic deficiency of SHED. ERK1/2 inhibitor treatment rescued bFGF-induced osteogenic differentiation deficiency. Conclusion: These data suggest that bFGF inhibits osteogenic differentiation of SHED via ERK1/2 pathway. Blockade ERK1/2 signaling by small molecular inhibitor treatment improves bone formation of SHED after bFGF treatment.